Monitoring the Depth of Anesthesia

13

Franco Cavaliere and Carlo Cavaliere

Contents

General anesthesia is a pharmacologically induced, fully reversible condition characterized by a depression of central nervous system functions aimed at achieving some goals necessary to perform a surgical or other procedure. These objectives include the loss of consciousness, analgesia, amnesia, the abolition of neurovegetative responses to stimuli, immobility, and, in some cases, the loss of muscle tone [1]. These effects are obtained through the administration of drugs. The concept of depth of anesthesia expresses the degree of depression of the central nervous system, which is a function of the concentration of anesthetics at the effector site and manifests itself with the abolition of responses to stimuli of increasing intensity. In 1937, Guedel classified the depth of anesthesia obtained with ethyl ether in four stages (analgesia, delirium, surgical anesthesia, and overdose), of which the third divided into four planes [2]. According to that scheme, each stage and plane were

F. Cavaliere (✉)
Department of Cardiovascular Sciences, Catholic University of the Sacred Heart, Rome, Italy
e-mail: f.cavaliere@rm.unicatt.it

C. Cavaliere
ENT Clinic, University "Sapienza", Rome, Italy

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identifiable through a series of signs related to the patient's respiratory activity and muscle tone, eye movements, pupil diameter, and the presence and intensity of the pupillary light reflex. The classification of Guedel refers to a monopharmacological anesthesia, obtained by administering increasing concentrations of ethyl ether. In modern anesthesia, however, the evaluation of the depth of anesthesia is made much more complicated by two aspects:

- When using a single drug, the goals of anesthesia are achieved at different anesthetic concentrations at the effector site. For example, loss of consciousness requires lower concentrations than the abolition of muscle tone. This process is well suited to classification like that of Guedel. In modern anesthesia, however, the desired effects are obtained with specific drugs. Thus, analgesia can be achieved with the use of opioids, muscle hypotonia with muscle relaxants, and loss of consciousness with hypnotics.
- The depth of anesthesia is a dynamic concept that reflects the balance between the degree of pharmacological depression and the intensity of the stimulus. Consequently, the same concentration of the anesthetic at the level of the effector site can be useful in one phase of the intervention and insufficient in another, more painful. The anesthesiologist's ability consists in maintaining a level of anesthesia adequate for the extent of the surgical stimulus in the different phases of the intervention.

Excessive depth of anesthesia increases the costs because it causes a higher consumption of drugs and a delay in the recovery of the state of consciousness at the end of the intervention. Some studies also suggest that an excessive depth of anesthesia is associated with more significant mortality and morbidity and a higher incidence of delirium and cognitive dysfunction in the postoperative period [3, 4]. On the contrary, inadequate depth of anesthesia prevents the attainment of its aims, such as the abolition of neurovegetative responses or the immobility of the patient. Particularly insidious is the persistence of the state of consciousness that underlies the phenomenon of awareness.

13.1 Awareness

Awareness, nowadays better defined as "accidental awareness during general anesthesia (AAGA)," is a condition of accidental and unwanted recovery of the state of consciousness during general anesthesia [5, 6]. It is a complication challenging to diagnose because the clinical signs related to the patient's movements and neurovegetative reactions in response to external stimuli may be lacking; this occurs more frequently when muscle relaxants are used to eliminate muscle tone and opioids to obtain adequate intraoperative analgesia [6].

The technique of the isolated forearm has been used for research purposes to highlight the persistence of the state of consciousness during general anesthesia [7]. For this purpose, after the induction of anesthesia and before the administration of the muscle relaxant, a cuff is inflated at the root of one of the upper limbs of the patient

until it reaches a pressure higher than the systolic blood pressure. In this way, we exclude the musculature of the arm from the action of the muscle relaxants, and it is possible to ask the anesthetized and paralyzed patient to shake the hand on command. With this technique, a high incidence of AAGA has been highlighted, around 4%, although the percentage was variable between studies [8]. These results do not correspond, however, to the extent of explicit memories of the intraoperative period, which fortunately are much less frequent. To explain this discrepancy, some authors have hypothesized that the ability to shake hands during the execution of the isolated forearm technique does not necessarily indicate the presence of a state of full consciousness. Instead, a condition of disanesthesia would be achieved [9], characterized by a perception of events lived in a neutral and disjoint way and separated from pain and emotion. Others have speculated that the amnesic effect of general anesthesia could inhibit the patient's ability to remember an episode of AAGA [10]. According to this hypothesis, anesthetic concentrations lower than those necessary for the abolition of the state of conscience may be sufficient to achieve amnesia. If this hypothesis was correct, the episodes of AAGA could be more frequent than those recorded in the interviews with the patients because they are fixed in the memory only in a small number of cases. This issue has ethical implications because the risk of episodes in which the patient is aware of what is happening during general anesthesia, even in the absence of memories and psychological relics, is probably unacceptable.

Apart from the technique of the isolated forearm, the diagnosis of AAGA is made in the postoperative period, after the recovery of consciousness. Under these conditions, the patient keeps memories of events that occurred during general anesthesia. These memories can be linked to explicit or implicit memory [11]. In the first case, the patient spontaneously remembers his/her experience, often with heavy emotional involvement. These are the cases that can be associated with significant psychological problems, such as post-traumatic stress disorder. When only implicit memory is affected, memories do not reach consciousness except through external stresses. Hypnosis can be very useful in this regard. In literature, however, most of the studies were performed with the administration of specific questionnaires, such as that of Brice, composed of six questions [12]. Sometimes, the memory of the AAGA can resurface with generic questions such as “Did you have problems with anesthesia?” included in the questionnaires aimed to evaluate the quality of the assistance received. However, the sensitivity toward the issue of awareness is much lower than that of the Brice questionnaire [13].

It is important to note that the frequency of AAGA is variable between the studies and depends mainly on the technique used for the detection. Thus the recent multicenter ConsCIOUS-1 study, conducted on 260 patients with the isolated forearm technique, showed the responsiveness of 4.6% of patients (one case every 22) to verbal commands at the time of intubation, without however any evidence of explicit memory of the episode [8]. In the SNAP-1 study (1st Sprint National Anesthesia Project), conducted on 16222 patients through a modified Brice questionnaire administered 24 h after anesthesia, AAGA incidence was 0.12%, i.e., one case every 800 patients [14]. Finally, assessments based on generic surveys, unstructured with specific questions for the AAGA research, estimated the awareness incidence of 1:19,600 cases, mostly related to explicit memory [9].

In general, the factors associated with an increased risk of AAGA are classifiable according to the patient, the procedure, and the anesthetics used [15, 16]. Since most cases of awareness are caused by an insufficient depth of anesthesia, patients with minor cardiorespiratory functional reserve, classifiable as ASA III and IV, are more prone to the AAGA due to the need to limit the dosage of the anesthetics. In contrast, patients with a history of substance abuse or chronic opioid intake may be more prone to AAGA because they have developed resistance to anesthetics. Finally, the increased risk of AAGA that characterizes patients who have already experienced similar episodes could be explained, in some cases, with higher resistance to anesthetics on a genetic pharmacodynamic or pharmacokinetic basis. Among the surgical interventions with a higher frequency of AAGA, there are those of cardiac surgery, cesarean section, and emergency surgery in multiple trauma patients. Concerning the drugs used, the AAGA occurs with a higher frequency when using muscle relaxants and in totally intravenous anesthesia; conversely, it is less frequent in inhalation anesthesia, probably due to the possibility of monitoring the end-expiratory concentration of anesthetic vapors. The analysis of AAGA cases with memories related to explicit memory provides other elements on the causes and the risk factors [9]. In two-thirds of them, the complication occurs in the induction or awakening phase. Often, it is possible to recognize the probable cause, such as a syringe mistake, the administration of the muscle relaxant before the hypnotic, the suspension of the hypnotic at the end of the operation when the muscular paralysis is still present, and the interruption of the hypnotic administration during transport in intensive care. In the maintenance phase of anesthesia, many episodes of AAGA are due to technical errors, such as not refilling an empty anesthetic vaporizer or excluding alarms on the end-expiratory concentration of anesthetics.

The consequences of AAGA are variable [16–18]. While the episodes associated with implicit memory generally do not cause disorders, those with explicit memory can cause substantial psychological alterations, characterized by states of anxiety, sleep disturbances, nightmares, sudden memories, and diseases of the working and relational life. Sometimes, the patient may develop an overt post-traumatic distress syndrome; in most cases, however, these are nonsevere syndromes that regress over time, as evidenced by studies conducted over the long term. The postoperative management of AAGA suggested by the American Society of Anesthesiologists in 2006 is divided into three phases [1]:

- the initial meeting with the patient consists of an interview characterized by a profound empathy, conducted preferably in the presence of witnesses and summarized in an accurate written report;
- verification of what reported by the patient to confirm the suspicion of AAGA and search for the probable cause;
- patient support, which includes further interviews with the anesthesiologist (i.e., 1 day after the first meeting and 2 weeks later), the request for psychological counseling, and possible pharmacological and psychotherapeutic treatments.

The prevention of AAGA includes all the measures aimed at avoiding errors or accidents, such as the control of the anesthetic apparatus and in particular of the vaporizers and the prevention of errors in the administration of drugs. The use of muscle relaxants should be limited to cases in which there is a clear indication and associated with the monitoring of the degree of myorelaxation to exclude the presence of a residual muscle paralysis at the end of anesthesia.

13.2 EEG and Anesthesia

EEG offers a noninvasive tool to analyze the activity of the cerebral cortex during general anesthesia [19]. The recorded electrical activity is indicative of the extracellular electrical potentials resulting from the degree of polarization of cortical neuron membranes and postsynaptic potentials. The paths obtained reflect the activity of the cerebral cortex and are only indirectly influenced by the subcortical areas, the potentials of which originate at a greater distance from the electrodes and are therefore of too low amplitude. EEG variations occurring during anesthesia reflect the action of anesthetics on various brain areas and in particular, the inhibition of the cerebral cortex activity and, indirectly, of the ascending reticular substance and the thalamus. At the induction and the subsequent deepening of anesthesia, we observe the following sequence (Table 13.1) [20]:

- The first phase of paradoxical excitation occurs at the induction and ends with the loss of consciousness. It is mostly characterized by beta activity and is associated with clinical signs of inhibition of cortical activity, such as uncontrolled movements, incoherent speeches, alteration of the perception of time, euphoria, or dysphoria.

Table 13.1 EEG patterns during general anesthesia [20]

Before induction, eyes closed		
Prominent alpha activity (10 Hz)		
Induction period		
Increase in beta activity on the EEG (13–25 Hz)		
Maintenance period		
Phase 1	Light anesthesia	Beta activity decreases, alpha (8–12 Hz) and delta (0–4 Hz) activities increase
Phase 2	Intermediate anesthesia	Further increase in alpha and delta activity in the anterior leads (anteriorization)
Phase 3	Deep anesthesia	Phases of absent electrical activity (burst suppression) alternated With alpha and beta activity
Phase 4	Most profound anesthesia	EEG is isoelectric
Emergence period		
EEG patterns proceed in approximately reverse order		

- Prevalence of alpha and delta rhythms on the beta rhythm is indicative of a condition of superficial anesthesia.
- A further accentuation of the prevalence of alpha and delta rhythms, especially in the anterior derivations, is associated with an intermediate level of anesthesia.
- Phases of absent electrical activity alternated with alpha and beta activity characterize the appearance of the phenomenon of burst suppression. This condition highlights the achievement of a deep level of anesthesia and is quantified by the burst suppression ratio, i.e., the percentage of time occupied by the isoelectric line. The burst suppression also occurs in other conditions, such as hypothermia, and represents the target of the pharmacological treatment of refractory epileptic illness and intracranial hypertension resistant to maximal medical therapy.
- The presence of an isoelectric pattern corresponds to a burst suppression ratio of 100.

The scheme mentioned above well describes the electroencephalographic changes induced by propofol or sevoflurane, and in general by the anesthetics that act on the GABAergic circuits. Drugs such as nitrous oxide and opioids cause electroencephalographic changes other than those described above. The administration of ketamine, which mainly works on NMDA receptors, is associated with an increase in beta and gamma activity (25–32 Hz) [21].

13.3 EEG Recording and Processing

The electrical potentials generated by the cerebral cortex are of intensity 100 times lower than those recorded with the electrocardiogram [22]. This poses the problem of the difficulty of isolating this electrical activity from the background noise, which includes sources internal to the organism and environmental sources [23]. Among the first is the electrical activity of the frontal and eye muscles; among the latter are the electrical potentials generated by the operating room equipment, such as the electric scalpel. The quality of the signal, then, depends on several factors, including environmental temperature and humidity and the conductivity of the patient's tissues. The electric potentials are recorded through electrodes with gels applied to the forehead surface. The signal is suitably filtered to eliminate artifacts and then converted from analog to digital. Digitization involves sampling by points to transform a continuous variable into a discrete one. This process takes place by dividing the recording time into basal units called epochs. The digitalized signal is then further analyzed to provide the operator with simple numerical parameters that summarize the characteristics of the electroencephalographic trace about the depth of anesthesia.

The procedure, very complicated and entrusted to proprietary algorithms, is based on some fundamental techniques [22]. The analysis of the signal trend over time (time domain) includes the research and quantization of the phenomenon of burst suppression. In the tracks, the abscissa axis corresponds to time. The analysis of the signal energy distribution requires that the recorded signal is broken down into the

frequencies of which it is composed (frequency domain). This process is comparable to the separation of white light in different colors through a crystal prism:

- The rapid Fourier transformation is the mathematical method which allows the recorded signal to be rapidly broken down into a series of sinus waves of different phases, amplitudes, and frequencies whose sum reproduces the signal itself. This analysis allows assigning an intensity and a phase to each frequency. These frequencies can be classified as gamma (over 25 Hz), beta (between 12 and 25 Hz), alpha (between 8 and 12 Hz), theta (between 4 and 7 Hz), or delta (between 1 and 4 Hz).
- The median frequency and the spectral edge frequency (SEF) synthesize energy distribution. The two parameters correspond, respectively, to the frequency that divides the power of the spectrum into two equal parts, and to that below which 95% of the power of the spectrum falls.
- Representations related to this type of analysis are easily recognizable because they show the frequencies on the abscissa. Traces that make appreciable the variations over time of the spectral distribution of energy require three-dimensional representations (frequency/energy/time) and are generally realized using diagrams in which time appears in abscissa, the frequencies in ordinate, and the power in a color scale. Tracks of this type are called Spectrograms.
- The bispectral analysis is so named because it uses two primary frequencies and the sum frequency of the two to obtain information regarding the signal intensity and its coherence, i.e., the phase correspondence in the three frequencies (bicoherence).
- The analysis of the entropy is based on the irregularity and randomness of the potential registered. Conceptually this corresponds to the observation that the deepening of anesthesia involves a progressive synchronization of cortical electrical activity.

13.4 Commercially Available Devices

The existing equipment differs mainly based on the algorithms used for the analysis of the electroencephalographic signal and for the parameters they provide to the operator [24, 25].

The brain monitor from Aspect Medical Systems, Inc. (Newton, MA, USA) uses a proprietary algorithm based on spectral and bispectral analysis and burst suppression to calculate the Bispectral Index (BIS), which can range from 0 to 100. Values between 80 and 100 correspond to the awake patient, those between 60 and 80 to a light/moderate sedation, those between 40 and 60 to general anesthesia, and those below 40 to a deep depression of the central nervous system; values close to 0 unveil the presence of an isoelectric pattern. The device also allows the visualization of one electroencephalographic derivation and provides the burst suppression ratio and the activity of the front muscles. The most advanced version allows bilateral recording, which enables an evaluation of the symmetry

of the signal and provides SEF and spectrogram. It can be used in adults and children and is the device for which the most significant number of clinical studies is available.

The module for the evaluation of entropy developed by Datex-Ohmeda, Inc. (Helsinki, Finland) uses spectral analysis to generate two indices, state entropy (SE) and response entropy (RE). The first is based on the analysis of frequencies between 8 and 32 Hz, varies between 0 and 100, and is indicative of the depth of hypnosis. The second is influenced by the activity of the frontal muscles, employs higher frequencies, up to 47 Hz, varies between 0 and 91, and is more indicative of responsiveness to stimuli and nociception. Values indicative of adequate anesthesia depth are between 40 and 60 for both indices. The system is validated for adults and pediatric patients over 2 years of age.

The Sedline monitor (Sedline Inc., San Diego, CA, USA) works with four electroencephalographic derivations and uses an algorithm that evaluates the heterogeneity of the signal, its coherence between the two hemispheres, the relationship between anterior and posterior cortical areas, and the percentage of burst suppression. The Patient State Index (PSI) ranges between 0 and 100, but values indicative of optimal anesthesia depth are between 25 and 50. The device also provides four electroencephalographic traces and bilateral spectrogram. It can be used in adults and children over 1 year of age.

The Cerebral State Monitor produced by Danmeter (Odenssee, Denmark) uses a single derivation to perform an analysis based on the spectrogram and the percentage of burst suppression. The Cerebral State Index (CSI) varies between 0 and 100; values between 40 and 60 correspond to an adequate depth of anesthesia, values between 60 and 80 to light anesthesia or sedation, and values between 10 and 40 to deep anesthesia. The device also provides the percentage of burst suppression and the electromyographic activity of the front muscles.

The Consciousness Monitor of Morpheus Medical (Barcelona, Spain) uses an electroencephalographic derivation and an algorithm that includes the analysis of frequencies, burst suppression, and system irregularity. It provides an LoC index (Level of consciousness) variable between 0 and 99, with a target value between 40 and 60, in addition to the percentage of burst suppression and the electromyographic activity of the frontal muscles.

The Narcotrend monitor (MonitorTechnik, Bad Bramstedt, Germany) analyzes one or two electroencephalographic derivations with an algorithm based on temporal and spectral analysis and the rate of burst suppression. It provides an EEG E0 index variable between 0 and 100, classifies the patient's status according to six possible conditions that vary from A (awake) to F (deep), and provides information on the electromyographic activity of the frontal muscles.

The NeuroSENSE System (NeuroWave Systems Inc., Cleveland Heights, OH, USA) uses bilateral monitoring to obtain a WAVCNS index (Wavelet Anesthetic Value for Central Nervous System) ranging from 1 to 100 for each cerebral hemisphere.

The SNAPII monitor (Nicolet Biomedical, Madison, WI, USA) uses an electroencephalographic derivation and two frequency bands, the low one between 0 and

20 and the high one between 80 and 420 Hz, to process a SNAP index between 0 and 100.

Finally, the qCON 2000 monitor (Quantium Medical, Barcelona, Spain) uses a single electroencephalographic channel. It is based on spectral analysis and on the percentage of burst suppression to process two indexes, both between 0 and 100. The qCON index is a measure of the depth of hypnosis, while the qNOX index measures the degree of nociception. The device also provides information on the electromyographic activity of the frontal muscles and the percentage of burst suppression.

13.5 Auditory Evoked Potential Monitoring

Acoustic evoked potentials are also used to monitor the depth of anesthesia. In the trace obtained with their recording, the latency of the waves makes it possible to distinguish early potentials (within 10 ms, generated at the level of the brain stem), medium ones (between 10 and 50 ms, corresponding to the thalamus and early cortical response), and late ones (between 50 and 80 ms, corresponding to the late cortical response). The evoked potentials are sensitive to the action of anesthetics, both intravenous and inhaled. With the deepening of anesthesia, there is an increase in their latency and a reduction in amplitude [26].

The only device on the market that uses auditory evoked potentials for monitoring the depth of anesthesia is the AEP Monitor (Odenssee, Denmark). Analyzing the medium latency potentials, it provides the AAI index (A-line auditory evoked potential index), based on auditory evoked potentials and the analysis of electroencephalographic frequencies. The calculation is based on the evoked potentials if the signal quality is good or on the EEG spectral analysis if the signal quality is not adequate. In the first case, it varies between 0 and 100, in the second between 0 and 60.

13.6 Indications to Monitoring the Anesthesia Depth

The main indication for the use of anesthesia-depth monitoring systems is the prevention of awareness. The extensive literature now available on the subject has specified two points [27]. The first is that such monitoring significantly reduces the incidence of awareness with explicit memories. The second is that, from this point of view, the anesthesia-depth monitoring systems do not offer significant advantages compared to monitoring the end-expiratory concentration of anesthetic vapors during inhalation anesthesia. On this basis, the Association of Anesthesiologists from Great Britain and Ireland recommends the use of anesthesia depth monitoring in patients undergoing intravenous anesthesia or in patients using muscle relaxants [28]. The Association reiterates that there is no currently conclusive evidence that the use of these monitoring systems reduces awareness episodes when the end-expiration concentration of anesthetic vapors is monitored and appropriate alarm

limits are set. The UK National Institute for Health and Care Excellence (NICE) suggests the use of BIS, E-Entropy, and Narcotrend in the case of patients at risk of overdosing or underdosing anesthetic drugs and in patients undergoing totally intravenous anesthesia [29].

Other potential advantages of monitoring the depth of anesthesia are the lower dosage of anesthetics and the shortening of the duration of awakening from anesthesia. In this regard, the authors of a recent meta-analysis concluded that the use of anesthesia-depth monitoring systems in deep sedation appears to be associated with a significant, but modest, reduction in the anesthetic dosage, but not to a minor latency of awakening at the end of sedation [30].

Finally, a recent Cochrane review concluded that the use of anesthesia-depth monitoring systems could reduce the incidence of delirium and postoperative cognitive dysfunction three months after surgery in patients over 60 years of age undergoing noncardiac and nonneurosurgical surgery [31]. This effect would be linked to the prevention of excessive depth of anesthesia.

13.7 Use in Critically Ill Patients

BIS has been used in intensive care units to monitor the depth of sedation, particularly in patients who are treated with muscle relaxants [32]. However, under these conditions, the BIS values are poorly correlated with the clinical scales of sedation depth, nor there are significant advantages related to its use on a number of parameters, such as mortality, the length of stay in the intensive care unit, the length of mechanical ventilation, the incidence of ventilator-associated pneumonia, or other adverse events [33].The BIS has been also employed:

- as a prognostic index after head trauma or cardiac arrest,
- to evaluate the responses of cortical activity to external stimuli in states of minimum consciousness,
- to highlight the onset of epileptic seizures in curarized patients,
- to guide the administration of sedatives until the appearance of burst suppression in the treatment of status epilepticus.

Overall, the evidence for these types of use is modest, and caution is suggested [34].

13.8 Evaluation of Antinociception

Monitoring systems based on electroencephalogram analysis evaluate the effects of anesthetics on the cerebral cortex and are mainly oriented to assess the state of consciousness. However, the processing of painful stimuli occurs primarily at the level of subcortical areas, such as the thalamus, the limbic system, and the brainstem [35]. The response to painful stimuli and the implicit memory partly depends on the

activity of subcortical areas and may be inadequately monitored by EEG-based monitoring. This consideration might explain why it is difficult to predict the patient's response to a painful stimulus such as tracheal intubation based on the scores provided by EEG-based monitoring. In recent years, the industry has made available a few monitors aimed at assessing the degree of antinociception achieved during general anesthesia [35]. Among the responses to painful stimuli due to the activity of the subcortical areas, those mediated by the neurovegetative nervous system and in particular by the sympathetic system are more constant and reliable [36].

The measurement of the electrical conductivity of the skin uses skin electrodes positioned on the palm of the hand and exploits the secretion of sweat generated by the sympathetic stimulation [37]. Sweat contains mainly water and electrolytes and therefore increases the electrical conductivity. This effect can be detected already 2 s after a painful stimulation not entirely abolished by antinociception.

The Surgical Stress Index (SSI) varies from 0 to 100 [38]. The algorithm used for its calculation considers two parameters: the amplitude of the wave recorded by photoplethysmography and the variations of the ECG RR interval. The width of the photoplethysmographic wave is a measure of the degree of vasoconstriction and therefore of the sympathetic tone, while the variations of the RR interval are affected by the action of the neurovegetative system on the activity of the sinoatrial node.

The respiratory arrhythmia is the heart rate variability in synchrony with **respiration**; as a consequence, heart rate increases during inspiration and decreases during expiration. It is a physiological phenomenon more marked in some individuals. During general anesthesia, the application of a pain stimulus in the presence of inadequate antinociception influences this arrhythmia. The Analgesia Nociception Index (ANI) is calculated with an algorithm that analyzes the variability of the heart rate with the breaths [39].

Pupillometry allows you to measure the pupillary diameter accurately. Painful stimulations induce an increase in the pupillary diameter (ciliospinal reflex), which can be measured as a response to standardized intensity stimulations. This technique was effective in measuring the degree of antinociception during general anesthesia and postoperative analgesia [40]. However, the evaluation is complicated because the neurological circuits concerned have not yet been fully identified, and some drugs such as the opioids interfere with the ciliospinal reflex.

13.9 Conclusions

Loss of consciousness and antinociception are the two effects that most characterize general anesthesia. Currently, useful tools based on the recording and processing of the electroencephalogram are available for monitoring the degree of depression of the cerebral cortex, and therefore the depth of anesthesia. These monitoring systems effectively prevent AAGA associated with explicit memories, the most dangerous form because important psychological relics often follow it.

In inhalation anesthesia, however, it is possible to monitor the end-expiratory concentration of anesthetic vapors, which is informative of the concentration at the effector site. This monitoring is equally effective than EEG-based monitors in preventing AAGA. The costs of electroencephalogram-based monitoring systems would, therefore, be justified only in totally intravenous anesthesia or in patients particularly at risk of AAGA, for example, because of the use of myorelaxants. Devices aimed at monitoring antinociception are based on sympathetic or pupillary responses to pain stimuli.

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